

L35 ANSWER 209 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1991:7266 HCAPLUS Full-text  
 DOCUMENT NUMBER: 114:7266  
 TITLE: Immunosuppressive fluorinated cyclosporin analogs.  
 INVENTOR(S): Durette, Philippe L.; Pessolano, Arsenio A.;  
 Kollonitsch, Janos; Witzel, Bruce E.  
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
 SOURCE: Brit. UK Pat. Appl., 56 pp.  
 CODEN: BAXXDU  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2227244	A1	19900725	GB 1990-1212	19900118
US 5227467	A	19930713	US 1991-693783	19910429
PRIORITY APPLN. INFO.:			US 1989-298712	A 19890119
			US 1987-81255	B2 19870803
OTHER SOURCE(S):	MARPAT 114:7266			
GI				

x9-x10-x11-x1-x2-x3  
 \*8-x7-x6-x5\_\_\_\_\_ \*4 I

AB The title compds. [I; X1 = NR2C[CH(OH)CHR1CH2XR]CO; X2 = (fluorinated) Abu, Ala, Nva, Ser, Thr, Val; X3 = Sar, D-MeAla; X4, X6, X9, X10 = (fluorinated) MeLeu, MeVal; X5 = (fluorinated) Val, Nva; X7 = (fluorinated) Aba, Abu, Phe; X8 = D-Ala; X11 = (fluorinated) MeVal, MeNva; X = S, SO, SO2, O, NH; R = H, alkyl, alkenyl, thioalkyl, (substituted) pyridyl, Ph, furyl, pyrrolyl, thienyl, etc.; R1 = alkyl; R2 = alkyl,

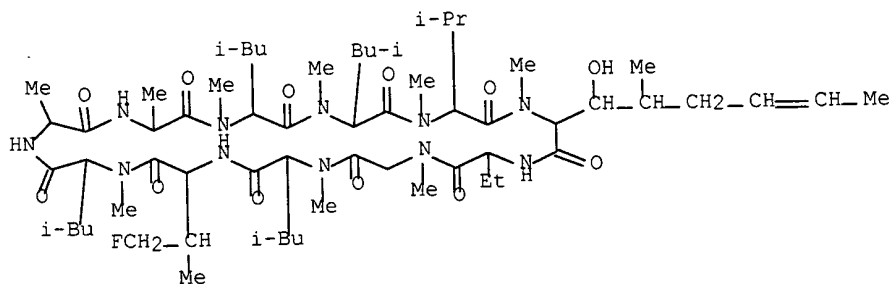
alkylphenyl], were prepared Thus, cyclo[[[(2S, 3R, 4R, 6E)-3-hydroxy-4- methyl-2- methylamino-6-octenoyl]-L-2-aminobutyryl-sarcosyl-N-methyl-L- leucyl-4-fluorovalyl-N- methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl- N-methyl-L-leucyl-N-methyl-L- valine] was prepared by the solution phase method using N,N-bis(2-oxo-3- oxazolidinyl)phosphorodiamidic chloride as a coupling agent. I had 10-163% of the T- cell proliferation inhibitory activity of cyclosporin A.

IT 121893-00-3P 130840-76-5P 130840-77-6P  
130840-78-7P 130840-79-8P 130840-80-1P  
130840-81-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of, as immunosuppressant)

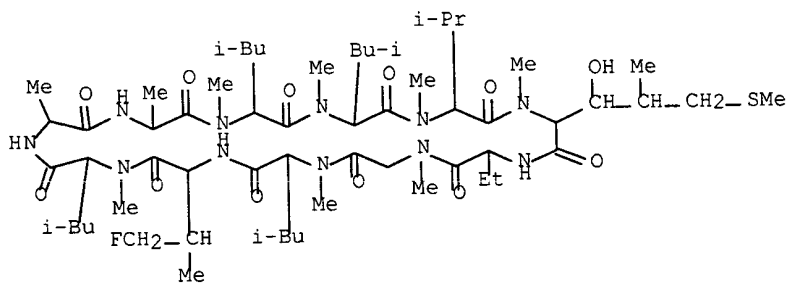
RN 121893-00-3 HCAPLUS

CN Cyclosporin A, 10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



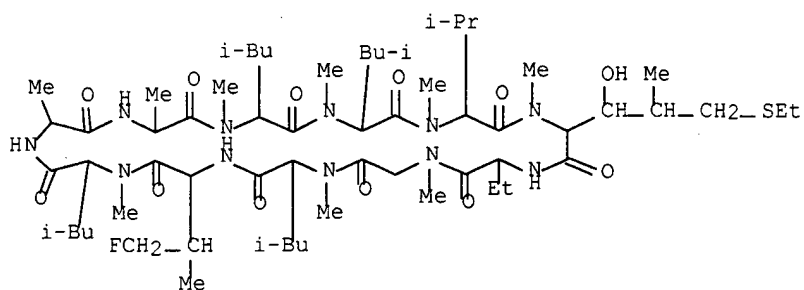
RN 130840-76-5 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-3-hydroxy-N-methyl-5-(methylthio)-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



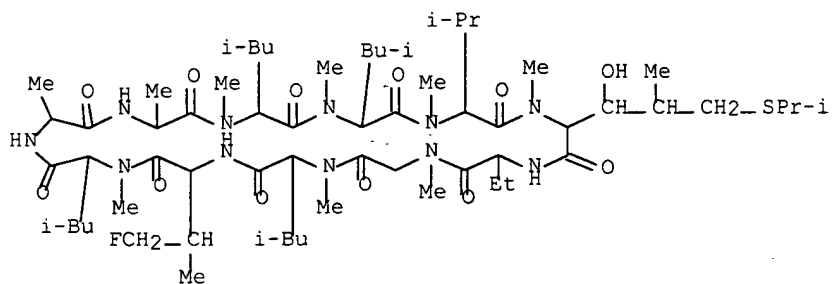
RN 130840-77-6 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-5-(ethylthio)-3-hydroxy-N-methyl-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



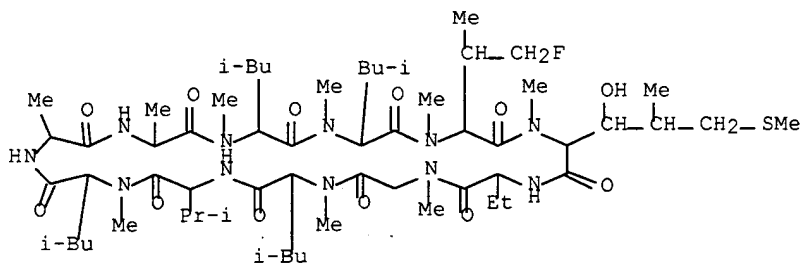
RN 130840-78-7 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-3-hydroxy-N-methyl-5-[(1-methylethyl)thio]-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



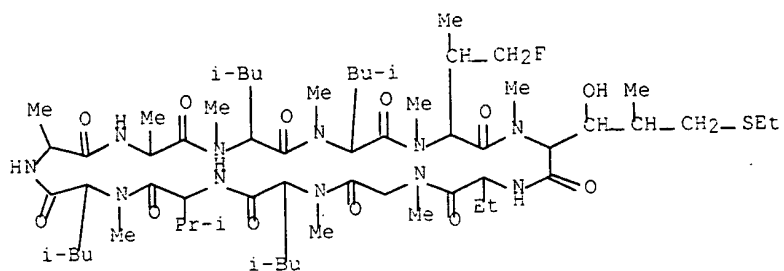
RN 130840-79-8 HCAPLUS

CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)-6-[(3R,4S)-3-hydroxy-N-methyl-5-(methylthio)-L-leucine]- (9CI) (CA INDEX NAME)



RN 130840-80-1 HCAPLUS

CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)-6-[(3R,4S)-5-(ethylthio)-3-hydroxy-N-methyl-L-leucine]- (9CI) (CA INDEX NAME)



RN 130840-81-2 HCAPLUS  
 CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)-6-[(3R,4S)-3-hydroxy-N-methyl-5-[(1-methylethyl)thio]-L-leucine]- (9CI) (CA INDEX NAME)

